

December 30, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (6576: Deep vein thrombosis and pulmonary embolism in cirrhotic patients: systematic review.doc).

Title: Deep vein thrombosis and pulmonary embolism in cirrhotic patients: systematic review

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6576

The manuscript has been improved according to the suggestions of reviewers:

Following revisions have been made according to the suggestions of the reviewer

(1) Reviewer 1:

- a. Abstract has been reformatted per Reviewer 1 suggestion. It has been updated to include Running Title, Author contributions and Core Tip.
- b. Art work (Table 1) has been included in the mechanism section to summarize the major factors affecting hemostasis in cirrhotic patients for easy readability.

(2) Reviewer 2:

- a. 3 new references have been added per suggestion, lines 84-86. Thank you for the suggestion.
- b. Minor changes to the verbiage under "Mechanism section" have been made as suggested. The only exception is that we have kept "Lines 119-121" from the original draft as we believe that the reference cited supports the original statement more closely as compared to the suggestion by the reviewer. However, we are willing to revise it if the reviewers feel otherwise.
- c. The last part of the last sentence under "Mechanism section" has been deleted as suggested: "thereby providing the direct evidence that Protein C deficiency seen in cirrhosis is associated with procoagulant state"
- d. In "Prevalence and risk factors", we have confirmed that the study by Ali et al (*Digestive diseases and sciences* 2011; 56(7): 2152-2159) included 449,798 hospitalizations for cirrhosis in 2005. We have updated the sentence to reflect that as compared to 449,798 cirrhotic patients. In the same para, following sentence has been added to support the preceding information "(36.7% of cirrhotics with VTE were age 65 years and older compared to 29.5% of cirrhotics without VTE (p < 0.001))." Line 240
- e. Last paragraph in "Risk Factors" has been modified to reflect minor changes, as suggested by the reviewer.
- f. In "Management Section, under Efficacy and Safety", we have kept our original draft opening line as we had difficulty understanding the reviewer's comment. We will be happy to revise it if needed. Line 306-307
- g. Line 336 has been rewritten as suggested "That no patients died from VTE related complications is of great importance"
Following lines have been deleted from the section - Management, Efficacy and Safety,

Para 5. "Decrease in Vitamin- K dependent Protein C on initiation of VKA therapy and thereby increasing the risk of thrombosis is an additional theoretical concern, which may be negated by overlapping with LMWH for first few days."

"However, further validation studies are required in cirrhotic patients, including those getting VKAs, before these tests can be used in clinical practice. Until then, the use of oral VKA agents may just be limited to well compensated cirrhotics with a completely normal INR with careful monitoring of INR during the treatment."

- h. In the last para in Management Section, "careful monitoring of anticoagulation management in the hands of coagulation experts" has been added as suggested by the reviewer at the end of the para to emphasize this important point. Line 420.
- i. Conclusions section has been modified to include reviewers suggestions.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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